AMENDMENTS TO THE CLAIMS

Please amend the following claims:

1. (original) A method of modulating microtubule polymerisation in a subject, said method comprising administering a therapeutically effective amount of at least one compound of the general formula (I)

I

or pharmaceutically acceptable prodrugs, salts, hydrates, solvates, crystal forms or diastereomers thereof, wherein:

R1 is H, C_{1-4} alkyl;

Q is a bond, or C_{1-4} alkyl;

A is aryl, hetaryl optionally substituted with 0-3 substituents independently chosen from halogen, C₁₋₄ alkyl, CH₂F, CHF₂, CF₃, CN, aryl, hetaryl, OCF₃, OC₁₋₄alkyl, OC₂₋₅alkylNR4R5, Oaryl, Ohetaryl, CO₂R4, CONR4R5, nitro, NR4R5, C₁₋₄ alkylNR4R5, NR6C₁₋₄alkylNR4R5, NR4COR5, NR6CONR4R5, NR4SO₂R5;

R4, R5 are each independently H, C_{1-4} alkyl, C_{1-4} alkyl cycloalkyl, C_{1-4} alkyl cyclohetalkyl, aryl, hetaryl, C_{1-4} alkyl aryl, C_{1-4} alkyl hetaryl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR7;

R6 is selected from H, C₁₋₄ alkyl;

R7 is selected from H, C_{1-4} alkyl, aryl, hetaryl, C_{1-4} alkyl aryl, C_{1-4} alkyl hetaryl;

R2 is 0-2 substituents independently selected from halogen, C₁₋₄alkyl, OH, OC₁₋₄alkyl, CH₂F, CHF₂, CF₃, OCF₃, CN, C₁₋₄alkylNR8R9, OC₁₋₄alkylNR8R9, CO₂R8, CONR8R9, NR8R9, NR8COR9, NR10CONR8R9, NR8SO₂R9;

R8, R9 are each independently H, C_{1-4} alkyl, C_{1-4} alkyl cycloalkyl, C_{1-4} alkyl cyclohetalkyl, aryl, hetaryl, C_{1-4} alkyl aryl, C_{1-4} alkyl hetaryl, or may be joined to form an

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optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR11;

R10 is selected from H, C₁₋₄ alkyl, aryl or hetaryl;

R11 is selected from H, C_{1-4} alkyl, aryl, hetaryl, C_{1-4} alkyl aryl, C_{1-4} alkyl hetaryl;

Y is halogen, OH, NR12R13, NR14COR12, NR14CONR12R13, N14SO₂R13;

R12 and R13 are each independently H, CH₂F, CHF₂, CF₃, CN, C₁₋₄ alkyl optionally substituted with OH, OC₁₋₄alkyl or NR15R16, cycloalkyl; cyclohetalkyl, C₁₋₄ alkyl cycloalkyl, C₁₋₄ alkyl cyclohetalkyl, or may be joined to form an optionally substituted 3-6 membered ring optionally containing an atom selected from O, S, NR14

R14, R15 and R16 are each independently selected from H, C_{1-4} alkyl; n = 0-4;

W is selected from H, C_{1-4} alkyl, C_{2-6} alkenyl; where C_{1-4} alkyl or C_{2-6} alkenyl may be optionally substituted with C_{1-4} alkyl, OH, OC_{1-4} alkyl, NR15R16;

R15, and R16 are each independently H, C_{1-4} alkyl, C_{1-4} alkyl cycloalkyl, C_{1-4} alkyl cyclohetalkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR17;

R17 is selected from H, C₁₋₄ alkyl.

2. (currently amended) A method according to claim 1 wherein the compound is selected from the group consisting of:

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<u>and</u>

- 3. (currently amended) A method according to claim 1 [[or claim 2]], wherein said method is used in the treatment of a hyperproliferation-related disorder or disease state.
- 4. (currently amended) A method according to claim [[2]] 3, wherein the hyperproliferation-related disorder or disease state is selected from the group consisting of [[Cancer]] cancer, infectious diseases, vascular restenosis and inflammatory diseases.
 - 5. (currently amended) A compound of the general formula (II)

$$A = \begin{bmatrix} R_1 & R_2 & R_3 & R_4 & R_5 & R_5$$

or pharmaceutically acceptable prodrugs, salts, hydrates, solvates, crystal forms or diastereomers thereof, wherein:

R1 is H, C_{1-4} alkyl;

Q is a bond, or C_{1-4} alkyl;

A is aryl, hetaryl optionally substituted with 0-3 substituents independently chosen from halogen, C₁₋₄ alkyl, CH₂F, CHF₂, CF₃, CN, aryl, hetaryl, OCF₃, OC₁₋₄alkyl, OC₂₋₅alkylNR4R5,

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Oaryl, Ohetaryl, CO₂R4, CONR4R5, nitro, NR4R5, C₁₋₄ alkylNR4R5, NR6C₁₋₄alkylNR4R5, NR4COR5, NR6CONR4R5, NR4SO₂R5;

R4, R5 are each independently H, C_{1-4} alkyl, C_{1-4} alkyl cycloalkyl, C_{1-4} alkyl cyclohetalkyl, aryl, hetaryl, C_{1-4} alkyl aryl, C_{1-4} alkyl hetaryl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR7;

R6 is selected from H, C₁₋₄ alkyl;

R7 is selected from H, C_{1-4} alkyl, aryl, hetaryl, C_{1-4} alkyl aryl, C_{1-4} alkyl hetaryl;

R2 is 0-2 substituents independently selected from C₁₋₄alkyl and OC₁₋₄alkyl;

Y is CH₂OH, OC₁₋₄alkylOH, OC₁₋₄alkylR12, OC₁₋₄alkylNR12NR13, C(O)R12, CH₂R12, COOR12, CONR12R13, OCONR12R13, CH₂NR12R13, NHCOR12, NHCONR12R13,

R12 and R13 are each independently H, C_{1-2} alkyl, $(CH_2)_3NEt_2$, $(CH_2)_2NMe_2$, $(CH_2)_5NH_2$, $(CH_2)_2OH$,

n = 0-4;

W is selected from H, C_{1-4} alkyl, C_{2-6} alkenyl; where C_{1-4} alkyl or C_{2-6} alkenyl may be optionally substituted with C_{1-4} alkyl, OH, OC_{1-4} alkyl, NR15R16;

R15, and R16 are each independently H, C_{1-4} alkyl, C_{1-4} alkyl cycloalkyl, C_{1-4} alkyl cyclohetalkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR17

R17 is selected from H, C_{1-4} alkyl; wherein when Y is CH_2R12 then R12 is not H, C_{1-2} alkyl.

6. (currently amended) A compound according to claim 5 selected from the group consisting of:

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7. (original) A compound of the general formula (III)

or pharmaceutically acceptable prodrugs, salts, hydrates, solvates, crystal forms or diastereomers thereof, wherein:

 X_1, X_2, X_3, X_4 are selected from the following:

- (i) X_1 and X_2 are N and X_3 and X_4 are C independently substituted with Y;
- (ii) X_1 and X_4 are N and X_2 and X_3 are C independently substituted with Y;
- (iii) X_1 and X_3 are N and X_2 and X_4 are C independently substituted with Y;
- (iv) X_2 and X_4 are N and X_1 and X_3 are C independently substituted with Y;
- (v) X_1 is N and X_2 , X_3 , and X_4 are C independently substituted with Y;
- (vi) X_3 is N and X_1 , X_2 , and X_4 are C independently substituted with Y;
- (vii) X_4 is N and X_1 , X_2 , and X_3 are C independently substituted with Y;
- (viii) X₂ is N and X₁, X₃, and X₄ are C independently substituted with Y; and
- (ix) X_1 , X_2 and X_3 are N and X_4 is C substituted with Y;

R1 is H, C_{1-6} alkyl, C_{1-6} alkylNR5R6, C_{1-6} alkylNR5COR6, C_{1-6} alkylNR5SO₂R6, C_{1-6} alkylCO₂R5, C_{1-6} alkylCONR5R6, where R5 and R6 are each independently H, C_{1-4} alkyl, aryl, hetaryl, C_{1-4} alkylaryl, C_{1-4} alkylhetaryl or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR7;

R7 is selected from H, C₁₋₄alkyl;

R2 is selected from C_{1-6} alkylOH, OC_{2-6} alkylOH, C_{1-6} alkylNR8R9, OC_{2-6} alkylNR8R9, C_{1-6} alkylNR8COR9, OC_{2-6} alkylNR8COR9, C_{1-6} alkylhetaryl, OC_{2-6} alkylhetaryl, OC

R8, R9 are each independently H, C₁₋₄alkyl, C₁₋₄alkylNR11R13, hetaryl, cyclohetalkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR14;

R12 is C₂₋₄alkyl, C₁₋₄alkylNR11R13, hetaryl, cyclohetalkyl;

R11, R13 are each independently H, C₁₋₄alkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR14;

R14 is selected from H, C₁₋₄alkyl;

R10 is H, C_{1-4} alkyl;

R3 and R4 are each independently H, halogen, C₁₋₄alkyl, OH, OC₁₋₄alkyl, CF₃, OCF₃; Q is a bond, or C₁₋₄ alkyl;

W is selected from H, C_{1-4} alkyl, C_{2-6} alkenyl; where C_{1-4} alkyl or C_{2-6} alkenyl may be optionally substituted with C_{1-4} alkyl, OH, OC_{1-4} alkyl, NR15R16;

R15, and R16 are each independently H, C₁₋₄alkyl, C₁₋₄alkyl cycloalkyl, C₁₋₄alkyl cyclohetalkyl, aryl, hetaryl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR17;

R17 is selected from H, C₁₋₄alkyl;

A is aryl, hetaryl optionally substituted with 0-3 substituents independently chosen from halogen, C₁₋₄ alkyl, CF₃, aryl, hetaryl, OCF₃, OC₁₋₄alkyl, OC₂₋₅alkylNR18R19, Oaryl, Ohetaryl, CO₂R18, CONR18R19, NR18R19, C₁₋₄ alkylNR18R19, NR20C₁₋₄alkylNR18R19, NR18COR19, NR20CONR18R19, NR18SO₂R19;

R18, R19 are each independently H, C_{1-4} alkyl, C_{1-4} alkyl cyclohetalkyl, aryl, hetaryl, C_{1-4} alkyl aryl, C_{1-4} alkyl hetaryl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR21;

R21 is selected from H, C₁₋₄alkyl;

R20 is selected from H, C₁₋₄alkyl;

Y is selected from H, C₁₋₄alkyl, OH, NR22R23;

R22, R23 are each independently H, C₁₋₄alkyl.

8. (original) A compound according to formula (III) of claim 7, wherein the compound is of the general formula (IV)

or pharmaceutically acceptable prodrugs, salts, hydrates, solvates, crystal forms or diastereomers thereof, wherein:

 X_1 , X_2 , X_3 , X_4 are selected from the following:

- (i) X_1 and X_2 are N and X_3 and X_4 are C independently substituted with Y;
- (ii) X_1 and X_4 are N and X_2 and X_3 are C independently substituted with Y;
- (iii) X_1 and X_3 are N and X_2 and X_4 are C independently substituted with Y;
- (iv) X_2 and X_4 are N and X_1 and X_3 are C independently substituted with Y;
- (v) X_1 is N and X_2 , X_3 , and X_4 are C independently substituted with Y;
- (vi) X_3 is N and X_1 , X_2 , and X_4 are C independently substituted with Y;
- (vii) X_4 is N and X_1 , X_2 , and X_3 are C independently substituted with Y;
- (viii) X₂ is N and X₁, X₃, and X₄ are C independently substituted with Y; and
- (ix) X_1 , X_2 and X_3 are N and X_4 is C substituted with Y;

R1 is H, C₁₋₆alkyl, C₁₋₆alkylNR5R6, where R5 and R6 are each independently H, C₁₋₄alkyl, aryl, hetaryl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR7;

R7 is selected from H, C₁₋₄ alkyl;

R2 is selected from C_{1-6} alkylOH, OC_{2-6} alkylOH, C_{1-6} alkylNR8R9, OC_{2-6} alkylNR8R9, C_{1-6} alkylNR8COR9, OC_{2-6} alkylNR8COR9, C_{1-6} alkylhetaryl, OC_{2-6} alkylhetaryl, OC

R8, R9 are each independently H, C₁₋₄alkyl, C₁₋₄alkylNR11R13, hetaryl, cyclohetalkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR14;

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R12 is C₂₋₄alkyl, C₁₋₄alkylNR11R13, hetaryl, cyclohetalkyl;

R11, R13 are each independently H, C₁₋₄alkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR14;

R14 is selected from H, C₁₋₄alkyl;

R10 is H, C₁₋₄alkyl;

R3 and R4 are each independently H, halogen, C₁₋₄alkyl, OH, OC₁₋₄alkyl, CF₃, OCF₃; Q is CH;

W is selected from C_{1-4} alkyl, C_{2-6} alkenyl; where C_{1-4} alkyl or C_{2-6} alkenyl may be optionally substituted with C_{1-4} alkyl, OH, OC_{1-4} alkyl, NR15R16;

R15, and R16 are each independently H, C₁₋₄alkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR17;

R17 is selected from H, C₁₋₄alkyl;

A is aryl, hetaryl optionally substituted with 0-2 substituents independently chosen from halogen, C₁₋₄ alkyl, CF₃, aryl, hetaryl, OCF₃, OC₁₋₄alkyl, OC₂₋₅alkylNR18R19, Oaryl, Ohetaryl, CO₂R18, CONR18R19, NR18R19, C₁₋₄ alkylNR18R19, NR20C₁₋₄alkylNR18R19, NR18COR19, NR20CONR18R19, NR18SO₂R19;

R18, R19 are each independently H, C_{1-4} alkyl, C_{1-4} alkyl cyclohetalkyl, aryl, hetaryl, C_{1-4} alkyl aryl, C_{1-4} alkyl hetaryl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR21;

R21 is selected from H, C₁₋₄alkyl;

R20 is selected from H, C₁₋₄alkyl;

Y is selected from H, C₁₋₄alkyl, NR22R23;

R22, R23 are each independently H, C₁₋₄alkyl.

9. (currently amended) A compound according to claim 7 wherein the compound is selected from the group consisting of:

10. (original) A compound of the general formula (V)

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or pharmaceutically acceptable prodrugs, salts, hydrates, solvates, crystal forms or diastereomers thereof, wherein:

 X_1 , X_2 , X_3 , X_4 are selected from the following:

(i) X_1 and X_2 are N and X_3 and X_4 are C independently substituted with Y;

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- (ii) X_1 and X_4 are N and X_2 and X_3 are C independently substituted with Y;
- (iii) X_2 and X_4 are N and X_1 and X_3 are C independently substituted with Y;
- (iv) X_1 is N and X_2 , X_3 , and X_4 are C independently substituted with Y;
- (v) X_3 is N and X_1 , X_2 , and X_4 are C independently substituted with Y;
- (vi) X_4 is N and X_1 , X_2 , and X_3 are C independently substituted with Y;
- (vii) X_2 is N and X_1 , X_3 , and X_4 are C independently substituted with Y; and
- (viii) X_1 , X_2 and X_3 are N and X_4 is C substituted with Y;

R1 is H, C₁₋₆alkyl, C₁₋₆alkylNR5R6, C₁₋₆alkylNR5COR6, C₁₋₆alkylNR5SO₂R6, C₁₋₆alkylCO₂R5, C₁₋₆alkylCONR5R6, where R5 and R6 are each independently H, C₁₋₄alkyl, aryl, hetaryl, C₁₋₄alkylaryl, C₁₋₄alkylhetaryl or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR7;

R7 is selected from H, C₁₋₄ alkyl;

R2 is selected from OH, OC₁₋₆alkyl, C₁₋₆alkylOH, OC₂₋₆alkylOH, C₁₋₆alkylNR8R9, OC₂₋₆alkylNR8R9, C₁₋₆alkylNR8COR9, OC₂₋₆alkylNR8COR9, C₁₋₆alkylhetaryl, OCONR8R9, NR8COR9, NR10CONR8R9, CONR8R9, NR8COR12;

R8, R9 are each independently H, C₁₋₄alkyl, C₁₋₄alkylNR11R13, hetaryl, cyclohetalkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR14;

R12 is C₂₋₄alkyl, C₁₋₄alkylNR11R13, hetaryl, cyclohetalkyl;

R11, R13 are each independently H, C₁₋₄alkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR14;

R14 is selected from H, C₁₋₄alkyl;

R10 is H, C_{1-4} alkyl;

R3 and R4 are each independently H, halogen, C₁₋₄alkyl, OH, OC₁₋₄alkyl, CF₃, OCF₃; Q is a bond, or C₁₋₄alkyl;

W is selected from H, C_{1-4} alkyl, C_{2-6} alkenyl; where C_{1-4} alkyl or C_{2-6} alkenyl may be optionally substituted with C_{1-4} alkyl, OH, OC_{1-4} alkyl, NR15R16;

R15, and R16 are each independently H, C₁₋₄alkyl, C₁₋₄alkyl cycloalkyl, C₁₋₄alkyl cyclohetalkyl, aryl, hetaryl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR17;

R17 is selected from H, C₁₋₄alkyl;

A is aryl, hetaryl optionally substituted with 0-3 substituents independently chosen from halogen, C₁₋₄ alkyl, CF₃, aryl, hetaryl, OCF₃, OC₁₋₄alkyl, OC₂₋₅alkylNR18R19, Oaryl, Ohetaryl, CO₂R18, CONR18R19, NR18R19, C₁₋₄ alkylNR18R19, NR20C₁₋₄alkylNR18R19, NR18COR19, NR20CONR18R19, NR18SO₂R19;

R18, R19 are each independently H, C_{1-4} alkyl, C_{1-4} alkyl cyclohetalkyl, aryl, hetaryl, C_{1-4} alkyl aryl, C_{1-4} alkyl hetaryl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR21;

R21 is selected from H, C₁₋₄ alkyl;

R20 is selected from H, C₁₋₄ alkyl;

Y is selected from H, C₁₋₄alkyl, OH, NR22R23;

R22, R23 are each independently H, C₁₋₄ alkyl.

11. (currently amended) A compound according to claim 10 selected from the group consisting of:

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12. (currently amended) A compound of the formula:

or a pharmaceutically acceptable prodrug, salt, hydrate, solvate, crystal form or a diastereomer thereof.

13. (canceled)

- 14. (currently amended) A composition comprising a carrier and at least one compound according to <u>claim 1</u> [[any one of claims 5 to 13]].
- 15. (currently amended) A method of treatment of a hyperproliferation-related disorder or disease state in a subject, said method comprising administering a therapeutically effective amount of at least one compound according to claim 1 [[any one claims 1 to 13 or a composition according to 14]].
- 16. (original) A method of treatment according to claim 15, wherein the hyperproliferation-related disorder or disease state is treatable by the modulation of microtubule polymerisation.
- 17. (currently amended) A method according to claim 15 [[or claim 16]], wherein the hyperproliferation-related disorder or disease state is selected from the group consisting of Cancer, infectious diseases, vascular restenosis or inflammatory diseases.
- 18. (currently amended) A method of treatment of a protein-kinase related disorder or disease state in a subject, said method comprising administering a therapeutically effective amount of at least one compound according to claim 1 [[any one of claims 1 to 13 or a composition according to 14]].

[[17.]] 19. (currently amended) A method according to claim 18, wherein the protein-kinase related disorder or disease state is selected from the group consisting of Atopy, Cell Mediated Hypersensitivity, Rheumatic Diseases, Other autoimmune diseases and Viral Diseases.

[[18.]] <u>20.</u> (currently amended) A method of treatment of diseases and conditions associated with inflammation and infection in a subject, said method comprising administering a therapeutically effective amount of at least one compound according to <u>claim 1</u> [[any one of <u>claims 1 to 13 or a composition according to claim 14]].</u>